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=> b reg
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DICTIONARY FILE UPDATES:   5 AUG 2007  HIGHEST RN 944042-79-9

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on property searching in REGISTRY, refer to:

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L2              STR
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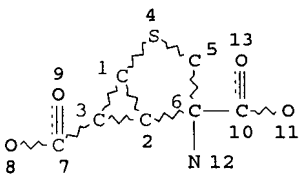


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.01


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FILE LAST UPDATED: 5 Aug 2007  (20070805/ED)
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitrn fhitstr l22 tot

L22 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:991499 HCAPLUS
DN 140:42463
TI Preparation of prodrugs of excitatory amino acids
IN **Moher, Eric David; Monn, James Allen;** Pedregal-Tercero, Concepcion
PA Eli Lilly and Company, USA; Collado, Cano Ivan; Blanco-Urgoiti, Jamie Gonzalo
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003104217	A2	20031218	2003WO-US15405	20030606 <--
	WO2003104217	A3	20040226		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
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	US2005222231	A1	20051006	2004US-0516559	20041130 <--
	IN2004KN01838	A	20060721	2004IN-KN01838	20041202 <--
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PRAI	2002EP-0380120	A	20020611 <--		
	2002EP-0380121	A	20020611 <--		
	2002US-415936P	P	20021003		
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	2003WO-US15405	W	20030606 <--		

OS MARPAT 140:42463
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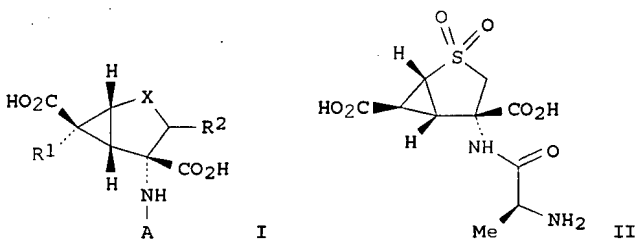


AB The invention relates to synthetic excitatory amino acid prodrugs for the treatment of neurol. disorders and psychiatric disorders. Bicyclic amino acids I [A is H-Q1-10, where Q is aminoacyl; X is O, S, SO, SO2, or substituted methylene; R1 is H or F; R2 is H, F, or OH] or their pharmaceutically-acceptable salts are claimed. Thus, prodrug II.HCl was prepared via peptide coupling reaction and shown to exhibit comparable concentration in rat plasma to that of the non-prodrug form.

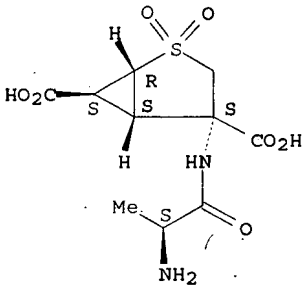
IT 635318-22-8P 635318-23-9P 635318-24-0P
635318-25-1P 635318-26-2P 635318-27-3P
635318-28-4P 635318-29-5P 635318-30-8P
635318-31-9P 635318-32-0P 635318-33-1P
635318-34-2P 635318-55-7P 635318-56-8P
635318-57-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of excitatory amino acids)

IT 635317-59-8P 635317-60-1P 635317-61-2P
635317-62-3P 635317-63-4P 635317-64-5P
635317-65-6P 635317-66-7P 635317-67-8P
635317-68-9P 635317-69-0P 635317-70-3P
635317-71-4P 635317-72-5P 635317-73-6P
635318-06-8P 635318-07-9P 635318-11-5P
635318-67-1P 635702-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of prodrugs of excitatory amino acids)

IT 635318-22-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of excitatory amino acids)

RN 635318-22-8 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, monohydrochloride, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=> d bib abs hitstr l23 tot

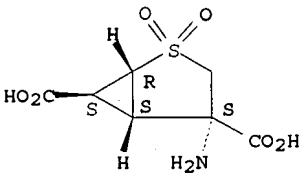
L23 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:635741 HCAPLUS
DN 147:110024
TI In vivo pharmacological characterization of the structurally novel, potent, selective mGlu2/3 receptor agonist LY404039 in animal models of psychiatric disorders
AU Rorick-Kehn, Linda M.; Johnson, Bryan G.; Knitowski, Karen M.; Salhoff, Craig R.; Witkin, Jeffrey M.; Perry, Kenneth W.; Griffey, Kelly I.; Tizzano, Joseph P.; **Monn, James A.**; McKinzie, David L.; Schoepp, Darryle D.
CS Neuroscience Discovery Research, Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, DC0510, Indianapolis, IN, 46285, USA
SO Psychopharmacology (Berlin, Germany) (2007), 193(1), 121-136
CODEN: PSCHDL; ISSN: 0033-3158
PB Springer GmbH
DT Journal
LA English
AB Data from both preclin. and clin. studies have provided proof of concept that modulation of limbic and forebrain glutamate, via mGlu2/3 receptor

agonists, might provide therapeutic benefits in many psychiatric disorders including schizophrenia and anxiety. The aim of this study was to assess the efficacy of a structurally novel, potent, selective mGlu2/3 receptor agonist with improved bioavailability (LY404039) in animal models predictive of antipsychotic and anxiolytic efficacy. LY404039 was assessed in amphetamine- and phencyclidine-induced hyperlocomotion, conditioned avoidance responding, fear-potentiated startle, marble burying, and rotarod behavioral tests. Monoamine release and turnover were assessed using microdialysis and ex vivo tissue levels. LY404039 attenuated amphetamine- and phencyclidine-induced hyperlocomotion (3-30 and 10 mg/kg, resp.). LY404039 (3-10 mg/kg) inhibited conditioned avoidance responding. LY404039 also reduced fear-potentiated startle in rats (3-30 μg/kg) and marble burying in mice (3-10 mg/kg), indicating anxiolytic-like effects. Importantly, LY404039 did not produce sedative effects or motor impairment as measured by rotarod performance and lack of escape failures in the conditioned avoidance task (at doses up to 30 and 10 mg/kg, resp.). LY404039 (10 mg/kg) also increased dopamine and serotonin release/turnover in the prefrontal cortex. These results demonstrate the broad preclin. efficacy of LY404039 across multiple animal models of antipsychotic and anxiolytic efficacy. Addnl., this compound modulates mesocortical neurotransmission and provides a novel mechanism for the treatment of psychiatric disorders that may be associated with improved efficacy and reduced incidence of undesirable side effects. As glutamatergic dysfunction has been linked to the etiol. of schizophrenia, clin. studies with more potent mGlu2/3 agonists, such as LY404039, may be useful to explore the validity of this hypothesis.

IT **635318-11-5**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vivo pharmacol. characterization of structurally novel, potent, selective mGlu2/3 receptor agonist LY404039 in animal models of psychiatric disorders)

RN 635318-11-5 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:400746 HCAPLUS
DN 146:372667
TI Pharmacological and pharmacokinetic properties of a structurally novel, potent, and selective metabotropic glutamate 2/3 receptor agonist: in vitro characterization of agonist (-)-(1R,4S,5S,6S)-4-amino-2-sulfonylbicyclo[3.1.0]-hexane-4,6-dicarboxylic acid (LY404039)
AU Rorick-Kehn, Linda M.; Johnson, Bryan G.; Burkey, Jennifer L.; Wright, Rebecca A.; Calligaro, David O.; Marek, Gerard J.; Nisenbaum, Eric S.; Catlow, John T.; Kingston, Ann E.; Giera, Deborah D.; Herin, Marc F.; **Monn, James A.**; McKinzie, David L.; Schoepp, Darryle D.
CS Neuroscience Discovery Research, Eli Lilly and Co., Indianapolis, IN, USA
SO Journal of Pharmacology and Experimental Therapeutics (2007), 321(1), 308-317
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Group II metabotropic glutamate (mGlu) receptor agonists, including (1S,2S,5R,6S)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylate monohydrate (LY354740) and (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY379268), have demonstrated efficacy in animal models of anxiety and

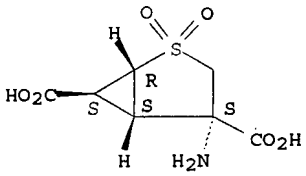
schizophrenia, and LY354740 decreased anxiety in human subjects. Herein, we report the in vitro pharmacol. profile and pharmacokinetic properties of another potent, selective, and structurally novel mGlu2/3 receptor agonist, (-)-(1R,4S,5S,6S)-4-amino-2-sulfonylbicyclo[3.1.0]hexane-4,6-dicarboxylic acid (LY404039) and provide comparisons with LY354740. Similar to LY354740, LY404039 is a nanomolar potent agonist at recombinant human mGlu2 and mGlu3 receptor (Ki = 149 and 92, resp.) and in rat neurons expressing native mGlu2/3 receptors (Ki = 88). LY404039 is highly selective for mGlu2/3 receptors, showing more than 100-fold selectivity for these receptors, vs. ionotropic glutamate receptors, glutamate transporters, and other receptors targeted by known anxiolytic and antipsychotic medications. Functionally, LY404039 potently inhibited forskolin-stimulated cAMP formation in cells expressing human mGlu2 and mGlu3 receptors. Electrophysiol. studies indicated that LY404039 suppressed elec. evoked excitatory activity in the striatum, and serotonin-induced L-glutamate release in the prefrontal cortex; effects reversed by LY341495. These characteristics suggest LY404039 modulates glutamatergic activity in limbic and forebrain areas relevant to psychiatric disorders; and that, similar to LY354740, it works through a mechanism that may be devoid of neg. side effects associated with current antipsychotics and anxiolytics. Interestingly, despite the slightly lower potency (.apprx.2-5-fold) of LY404039 vs. LY354740 in binding, functional, and electrophysiol. assays, LY404039 demonstrated higher plasma exposure and better oral bioavailability in pharmacokinetic expts. Collectively, the current data indicate that LY404039 may be valuable in the treatment of neuropsychiatric disorders, including anxiety and psychosis.

IT **635318-11-5**, LY 404039
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. and pharmacokinetic properties of metabotropic glutamate 2/3 receptor agonist LY404039)

RN 635318-11-5 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2006:1341533 HCAPLUS

DN 146:251680

TI Synthesis and Metabotropic Glutamate Receptor Activity of S-Oxidized Variants of (-)-4-Amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylate: Identification of Potent, Selective, and Orally Bioavailable Agonists for mGlu2/3 Receptors

AU **Monn, James A.**; Massey, Steven M.; Valli, Matthew J.; Henry, Steven S.; Stephenson, Gregory A.; Bures, Mark; Herin, Marc; Catlow, John; Giera, Deborah; Wright, Rebecca A.; Johnson, Bryan G.; Andis, Sherri L.; Kingston, Ann; Schoepp, Darryle D.

CS Discovery Chemistry and Neuroscience Research Divisions, Eli Lilly and Company, Indianapolis, IN, 46285, USA

SO Journal of Medicinal Chemistry (2007), 50(2), 233-240
CODEN: JMCMAR; ISSN: 0022-2623

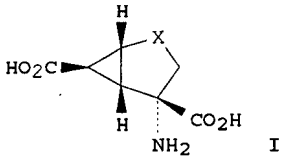
PB American Chemical Society

DT Journal

LA English

OS CASREACT 146:251680

GI



I

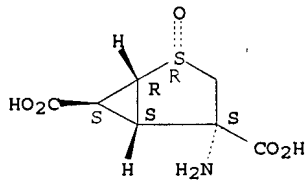
AB (-)-4-Amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylate (-)-I (X = S) (LY389795) is a highly potent and selective agonist of metabotropic glutamate receptors 2 (mGlu2) and 3 (mGlu3). As part of the ongoing research program, S-oxidized variants of this compound, namely both S-stereoisomers of I (X = SO) and I (X = SO2), were synthesized. Each of these chiral heterobicyclic amino acids displaced specific binding of the mGlu2/3 receptor antagonist 3H-2S-2-amino-2-(1S,2S-2-carboxycycloprop-1-yl)-3-(xanth-9-yl)propanoic acid (3H-LY341495) from membranes expressing recombinant human mGlu2 or mGlu3 and acted as potent agonists in cells expressing these receptor subtypes. Docking of the most potent of these derivs., (SR)-(+)-I [X = SO, (II)] to mGlu2 revealed the possibility of an addnl. H-bond interaction between the sulfoxide oxygen of II with tyrosine residue Y236. Pharmacokinetic anal. of mGlu active enantiomers II and (-)-I (X = SO2) in rats showed each to be well absorbed following oral administration. Consistent with their mGlu2/3 agonist potency and pharmacokinetic properties, both II and (-)-I (X = SO2) blocked phencyclidine-evoked ambulations in a dose-dependent manner, indicating their potential as nonclassical antipsychotic agents.

IT **926291-20-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure and mol. modeling; synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as orally bioavailable agonists for mGlu2/3 receptors)

RN 926291-20-5 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2-oxide, (1R,2R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

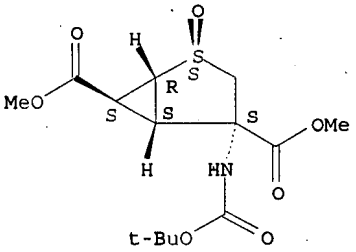


IT **926291-16-9P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystal structure; synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)

RN 926291-16-9 HCAPLUS

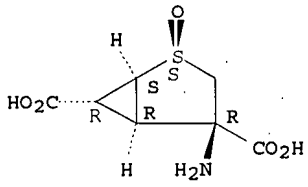
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(1,1-dimethylethoxy)carbonyl]amino]-, 4,6-dimethyl ester, 2-oxide, (1R,2S,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



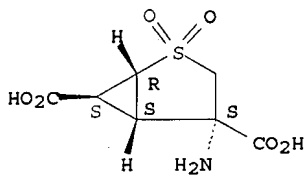
IT **926291-14-7**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)
RN 926291-14-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2-oxide, (1S,2S,4R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



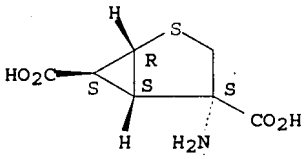
IT **635318-11-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)
RN 635318-11-5 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



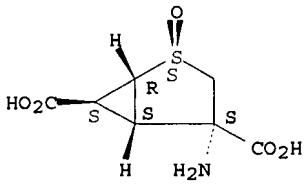
IT **222529-89-7**
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



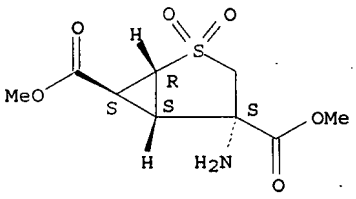
IT **926291-19-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)
RN 926291-19-2 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2-oxide, (1R,2S,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



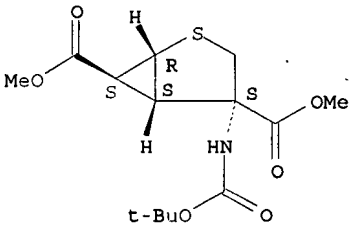
IT **635317-62-3P 926291-15-8P 926291-17-0P**
926291-18-1P 926291-21-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and metabotropic glutamate receptor activity of S-oxidized derivs. of (-)-4-amino-2-thiabicyclo-[3.1.0]hexane-4,6-dicarboxylic acid as selective and orally bioavailable agonists for mGlu2/3 receptors)
RN 635317-62-3 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 4,6-dimethyl ester, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



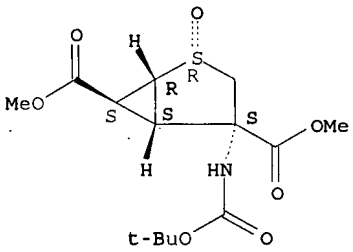
RN 926291-15-8 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(1,1-dimethylethoxy)carbonyl]amino]-, 4,6-dimethyl ester, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



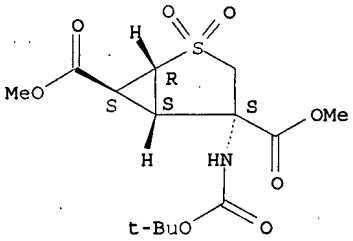
RN 926291-17-0 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(1,1-dimethylethoxy)carbonyl]amino]-, 4,6-dimethyl ester, 2-oxide, (1R,2R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



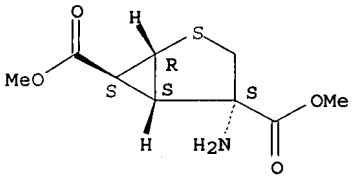
RN 926291-18-1 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(1,1-dimethylethoxy)carbonyl]amino]-, 4,6-dimethyl ester, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 926291-21-6 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 4,6-dimethyl ester, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:761719 HCAPLUS
DN 143:279124

TI Analgesic effects of the selective group II (mGlu2/3) metabotropic glutamate receptor agonists LY379268 and LY389795 in persistent and inflammatory pain models after acute and repeated dosing

AU Jones, Carrie K.; Eberle, Elizabeth Lutz; Peters, Stephen C.; **Monn, James A.**; Shannon, Harlan E.

CS Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA

SO Neuropharmacology (2005), 49(Suppl. 1), 206-218
CODEN: NEPHBW; ISSN: 0028-3908

PB Elsevier B.V.

DT Journal

LA English

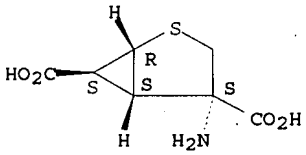
AB Group II (mGluR2/3) metabotropic glutamate receptors have been implicated in the mechanisms of persistent pain states. In the present study, the effects of the selective group II metabotropic glutamate receptor agonists LY379268 and LY389795 were evaluated in the formalin test, carrageenan-induced thermal hyperalgesia and mech. allodynia, and capsaicin-induced mech. allodynia in rats. The agonists LY379268 and LY389795 produced dose-dependent decreases in formalin-induced behaviors that were antagonized by the mGlu2/3 receptor antagonist LY341495. The group II antagonist LY341495 produced parallel shifts in the LY379268 dose-response curve, consistent with a competitive antagonism. LY379268 decreased formalin-induced behaviors after intracisternal but not intrathecal administration, suggesting primarily a supraspinal site of action. Both LY379268 and LY389795 produced a dose-related reversal of carrageenan-induced thermal hyperalgesia and capsaicin-induced mech. allodynia, but had no effect on carrageenan-induced mech. allodynia. Both agonists also increased response latencies in the hot plate test, but were without effect in the tail-flick test. However, both agonists produced motor impairment on the inverted screen at doses that were analgesic. Moreover, tolerance to the analgesic effects of LY379268 developed after 4 days of once-daily repeated administration in the formalin, carrageenan, capsaicin and hot plate tests. The present findings indicate that group II (mGluR2/3) metabotropic glutamate receptors may be involved in the mechanisms of hyperalgesia and allodynia, however tolerance rapidly develops to these effects.

IT **222529-89-7**, LY389795
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic effects of LY379268 and LY389795 in persistent and inflammatory pain models)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:714957 HCAPLUS

DN 144:274498

TI The synthesis of isotopically labeled (+)-2-aminobicyclo[3.1.0]hexane-2,6-carboxylic acid and its 2-oxa- and 2-thia-analogs

AU Wheeler, William J.; O'Bannon, Douglas D.; Kennedy, Joseph H.; **Monn, James A.**; Tharp-Taylor, Roger W.; Valli, Matthew J.; Kuo, Fengjiun

CS Lilly Research Laboratories, A Division of Eli Lilly and Company, Indianapolis, IN, 46285, USA

SO Journal of Labelled Compounds & Radiopharmaceuticals (2005), 48(8), 605-620
CODEN: JLCRD4; ISSN: 0362-4803

PB John Wiley & Sons Ltd.

DT Journal

LA English

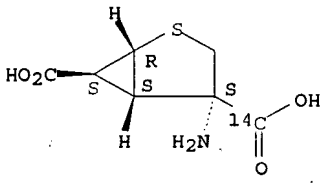
AB As part of a program aimed at the design of conformationally constrained analogs of glutamic acid, (+)-2-aminobicyclo[3.1.0]hexane-2,6-carboxylic acid (I), identified as a highly potent, selective, group II metabotropic glutamate receptor agonist was synthesized and studied clin. Heterocyclic analogs of I were subsequently synthesized in which the C(2) methylene was replaced by an oxygen atom (II) or a sulfur atom (III). Carbon-14-labeled isotopomers of I-III were synthesized to facilitate pre-clin. ADME studies. A tritium-labeled isotopomer of I was also synthesized for use in in vitro expts. A stable labeled isotopomer of rac-I was prepared for use as an internal standard for bioanal. assays. The key step in each of these syntheses was the reaction of 2-oxobicyclo[3.1.0]hexane-6-carboxylic acid (IV) or the appropriate aza or thia compound with K14CN/(NH4)2CO3 using the Bucherer-Berg protocol. In the preparation of the stable labeled isotopomer, rac-IV-[13C2] was prepared in two steps from Et bromoacetate-[UL-13C2]. Subsequent reaction of rac-IV-[13C2] with K13CN/15NH4Cl/Na2CO3, followed by hydrolysis of the hydantoin yielded rac-I-[13C3,15N].

IT **878283-10-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of isotopically labeled aminobicyclo[3.1.0]hexanecarboxylate and oxa and thia analogs)

RN 878283-10-4 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic-4-14C acid, 4-amino-, (1R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:531823 HCAPLUS

DN 137:232888

TI (2S,1'S,2'S,3'R)-2-(2'-Carboxy-3'-methylcyclopropyl)Glycine Is a Potent and Selective Metabotropic Group 2 Receptor Agonist with Anxiolytic Properties

AU Collado, Ivan; **Pedregal, Concepcion**; Mazon, Angel; Felix Espinosa, Juan; Blanco-Urgoiti, Jaime; Schoepp, Darryle D.; Wright, Rebecca A.; Johnson, Bryan G.; Kingston, Ann E.

CS Lilly SA, Madrid, 28108, Spain

SO Journal of Medicinal Chemistry (2002), 45(17), 3619-3629
CODEN: JMCMAR; ISSN: 0022-2623

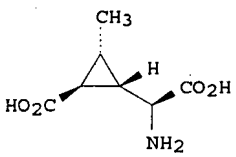
PB American Chemical Society

DT Journal

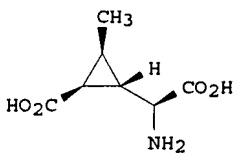
LA English

OS CASREACT 137:232888

GI



I



II

AB The asym. synthesis and biol. activity of (2S,1'S,2'S,3'R)-2-(2'-carboxy-3'-methylcyclopropyl)glycine I and its epimer II (at the C3' center) are described. I is a highly potent and selective agonist for group 2 metabotropic glutamate receptors (mGluRs). It is also systemically 4 orders of magnitude more active in the fear-potentiated startle model of

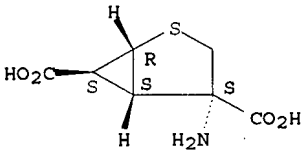
anxiety in rats than the rigid constrained bicyclic system LY354740. In summary, the authors have shown that high mol. complexity of conformationally constrained bicyclic systems is not a requirement to achieve highly selective and potent group 2 mGluRs agonists.

IT **222529-89-7**, LY 389795
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity comparisons of [(carboxy)(methyl)cyclopropyl]glycine with other selective agonists of metabotropic glutamate receptors)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:74530 HCAPLUS

DN 132:217391

TI Neuroprotective actions of novel and potent ligands of group I and group II metabotropic glutamate receptors

AU Kingston, A. E.; O'Neill, M. J.; Bond, A.; Bruno, V.; Battaglia, G.; Nicoletti, F.; Harris, J. R.; Clark, B. P.; **Monn, J. A.**; Lodge, D.; Schoepp, D. D.

CS Eli Lilly and Co. Ltd., Windlesham, Surrey, GU20 6PH, UK

SO Annals of the New York Academy of Sciences (1999), 890(Neuroprotective Agents), 438-449
CODEN: ANYAA9; ISSN: 0077-8923

PB New York Academy of Sciences

DT Journal

LA English

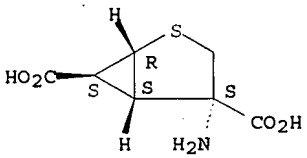
AB The role of group I metabotropic glutamate (mGlu) receptors in neurodegeneration is controversial because of the contradictory effects of mGlu1/5 agonists in in vitro models of neuronal cell death. In this study, novel and selective antagonists of mGlu1 and mGlu5: LY367385 and LY367366 were found to show consistent neuroprotective effects against N-methyl-D-aspartate (NMDA)-induced excitotoxicity in vitro and in vivo. Furthermore, intraventricular administration of LY367385 reduced hippocampal cell death in gerbils subjected to transient global ischemia. Previous studies have also shown that activation of group II mGlu receptors may contribute to neuroprotective mechanisms in vitro and in vivo. Three potent group II mGlu agonists-LY354740, LY379268 and LY389795-were found to attenuate both NMDA excitotoxicity and staurosporine-induced neuronal cell death. LY354740 and LY379268 were protective against transient global ischemia in gerbils when dosed i.p. These results support the view that antagonists of mGlu1 and mGlu5 and agonists of group II mGlu receptors may be useful agents in the therapeutic treatment of neurodegenerative disease.

IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective actions of novel and potent ligands of group I and group II metabotropic glutamate receptors)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(CA INDEX NAME)

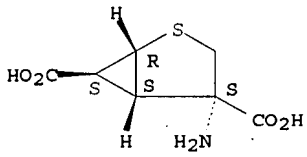
Absolute stereochemistry. Rotation (-).



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:546800 HCAPLUS
DN 131:281408
TI Neuroprotection by metabotropic glutamate receptor agonists: LY354740, LY379268 and LY389795
AU Kingston, Ann E.; O'Neill, Michael J.; Lam, Amy; Bales, Kelly R.; **Monn, James A.**; Schoepp, Darryle D.
CS Eli Lilly, Lilly Research Centre, Windleshanz, Surrey, GU20 6PH, UK
SO European Journal of Pharmacology (1999), 377(2/3), 155-165
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB In rat cortical neuronal cultures, metabotropic glutamate (mGlu) receptor agonists: LY354740 (+)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylate; LY379268 (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate, and LY389795 (-)-2-thia-4-aminobicyclo[3.1.0]- hexane-4,6-dicarboxylate, were neuroprotective against toxicity induced by N-methyl-D-aspartic acid (NMDA), kainic acid and staurosporine as measured by release of lactate dehydrogenase (LDH) activity into culture supernatants and DNA fragmentation by oligonucleosome formation. The potencies of the agonists were at least 100 times greater in reducing nucleosome formation than LDH release indicating a differential effect on neurons dying by apoptosis than by necrosis. In vivo studies showed that LY354740 was able to mediate a partial protection against apoptosis in CA1 hippocampal cells under ischemic conditions where substantial CAI cell loss occurred. The effects of the agonists in vitro were: (a) reversed by mGlu receptor antagonist LY341495, (b) enhanced by the presence of glial cells, (c) abrogated by RNA and protein synthesis inhibitors, and (d) unaltered by inhibition of endogenous adenosine activity. These results suggest that group 11 mGlu receptor agonists may represent a novel therapeutic strategy for the treatment of neurodegenerative diseases.
IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotection by metabotropic glutamate receptor agonists LY354740, LY379268 and LY389795)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:137687 HCAPLUS
DN 130:282320
TI Synthesis, Pharmacological Characterization, and Molecular Modeling of Heterobicyclic Amino Acids Related to (+)-2-Aminobicyclo[3.1.0]hexane-2,6-

dicarboxylic Acid (LY354740): Identification of Two New Potent, Selective, and Systemically Active Agonists for Group II Metabotropic Glutamate Receptors

AU **Monn, James A.**; Valli, Matthew J.; Massey, Steven M.; Hansen, Marvin M.; Kress, Thomas J.; Wepsiec, James P.; Harkness, Allen R.; Grutsch, John L., Jr.; Wright, Rebecca A.; Johnson, Bryan G.; Andis, Sherri L.; Kingston, Ann; Tomlinson, Rosemarie; Lewis, Richard; Griffey, Kelly R.; Tizzano, Joseph P.; Schoepp, Darryle D.

CS Discovery Chemistry Process Research and Development Neuroscience and Toxicology Research Divisions, Eli Lilly and Company, Indianapolis, IN, 46285, USA

SO Journal of Medicinal Chemistry (1999), 42(6), 1027-1040
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

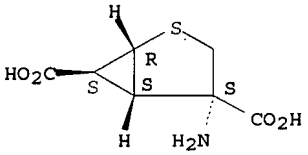
AB As part of an ongoing research program aimed at the identification of highly potent, selective, and systemically active agonists for group II metabotropic glutamate (mGlu) receptors, novel heterobicyclic amino acids (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY379268, I) and (-)-2-thia-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY389795, II) have been prepared I and II are structurally related to the previously described nanomolar potency group II mGlu receptor agonist, (+)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylate monohydrate (LY354740 monohydrate, III), with the C(4)-methylene unit of III being replaced with either an oxygen atom or a sulfur atom. I and II potently and stereospecifically displaced specific binding of the mGlu2/3 receptor antagonist ([3H]LY341495) in rat cerebral cortical homogenates, displaying IC50 values of 15 ± 4 and 8.4 ± 0.8 nM, resp., while having no effect up to 100,000 nM on radioligand binding to the glutamate recognition site on NMDA, AMPA, or kainate receptors. I and II also potently displaced [3H]LY341495 binding from membranes expressing recombinant human group II mGlu receptor subtypes: I Ki = 14.1 ± 1.4 nM at mGlu2 and 5.8 ± 0.64 nM at mGlu3; II Ki = 40.6 ± 3.7 nM at mGlu2 and 4.7 ± 1.2 nM at mGlu3. Evaluation of the functional effects of I and II on second-messenger responses in nonneuronal cells expressing human mGlu receptor subtypes demonstrated each to be a highly potent agonist for group II mGlu receptors: I EC50 = 2.69 ± 0.26 nM at mGlu2 and 4.58 ± 0.04 nM at mGlu3; II EC50 = 3.91 ± 0.81 nM at mGlu2 and 7.63 ± 2.08 nM at mGlu3. In contrast, neither compound (up to 10,000 nM) displayed either agonist or antagonist activity in cells expressing recombinant human mGlu1a, mGlu5a, mGlu4a, or mGlu7a receptors. The agonist effects of I and II at group II mGlu receptors were not totally specific, however, as mGlu6 agonist activity was observed at high nanomolar concns. for I (EC50 = 401 ± 46 nM) and at micromolar concns. (EC50 = 2 430 ± 600 nM) for II; furthermore, each activated mGlu8 receptors at micromolar concns. (EC50 = 1 690 ± 130 and 7 340 ± 2 720 nM, resp.). I.p. administration of either I or II in the mouse resulted in a dose-related blockade of limbic seizure activity produced by the nonselective group I/group II mGluR agonist (1S,3R)-ACPD (I ED50 = 19 mg/kg, II ED50 = 14 mg/kg), indicating that these mols. effectively cross the blood-brain barrier following systemic administration and suppress group I mGluR-mediated limbic excitation. Thus, I and II are novel pharmacol. tools useful for exploring the functions of mGlu receptors in vitro and in vivo.

IT **191471-53-1P 222529-89-7P 222529-90-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of aminooxa- and -thiabicyclohexanedicarboxylates as group II metabotropic glutamate receptor agonists)

RN 191471-53-1 HCAPLUS

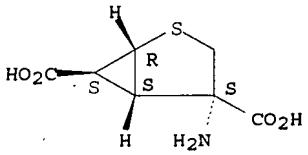
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



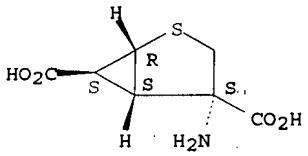
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 222529-90-0 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-,
(1R,4S,5S,6S)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

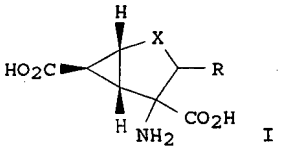


RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

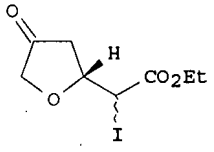
L23 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:752747 HCAPLUS
DN 127:359103
TI Preparation of bicyclic excitatory amino acid derivatives
IN Massey, Steven Marc; **Monn, James Allen**; Valli, Matthew John
PA Eli Lilly and Co., USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US---5688826	A	19971118	1996US-0749140	19961114
PRAI 1996US-0749140		19961114		

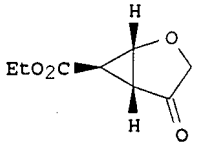
OS MARPAT 127:359103
GI



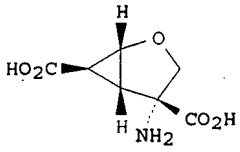
I



II



III



IV

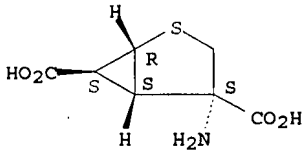
AB Title compds. I [X = O, NR1, S, S(O), SO2; R = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, (un)substituted aromatic group, (un)substituted heteroarom. group, non-aromatic carbocyclic group, non-aromatic heterocyclic group, non-aromatic monocyclic carbocyclic group fused with 1-2 monocyclic aromatic or heteroarom. groups, non-aromatic monocyclic heterocyclic group fused with 1-2 monocyclic aromatic or heteroarom. groups, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl substituted by 0-3 (un)substituted aromatic groups, (un)substituted heteroarom. groups, non-aromatic carbocyclic groups, non-aromatic heterocyclic groups, non-aromatic monocyclic carbocyclic group fused with 1-2 monocyclic aromatic or heteroarom. groups, non-aromatic monocyclic heterocyclic group fused with 1-2 two monocyclic aromatic or heteroarom. groups; R1 = H, (CO)nR; n = 0-1], non-toxic metabolically labile esters or amides thereof, and pharmaceutically acceptable salts thereof are useful as modulators of metabotropic glutamate receptor function. Thus, selective ketalization of (S)-(-)-1,2,4-butanetriol with acetone, followed by oxidation, Wittig olefination with (carbethoxymethylene)triphenylphosphorane, deprotection, iodolactonization, and oxidation gave tetrahydrofuranylacetate II. Treatment of II with DBU in EtOAc gave oxabicyclo[3.1.0]hexanonecarboxylate III, which was converted into title compound IV via spirohydantoin formation with (NH4)2CO3 and KCN, followed by basic hydrolysis and saponification formulations containing I are also given.

IT **191471-53-1P 191471-54-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic excitatory amino acid derivs.)

RN 191471-53-1 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

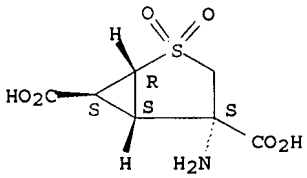
Relative stereochemistry.



RN 191471-54-2 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2,2-dioxide, (1α,4β,5α,6α)- (9CI) (CA INDEX NAME)

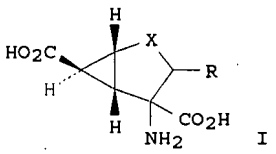
Relative stereochemistry.



L23 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:443241 HCAPLUS
DN 127:66216
TI Preparation of excitatory amino acid derivatives
IN **Monn, James Allen**; Valli, Matthew John; Massey, Steven Marc
PA Eli Lilly and Co., USA
SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP----774461	A1	19970521	1996EP-0308216	19961114
	EP----774461	B1	20060308		
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA---2237910	A1	19970522	1996CA-2237910	19961112
	CA---2237910	C	20051227		
	WO---9718199	A1	19970522	1996WO-US18112	19961112
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU---9677279	A	19970605	1996AU-0077279	19961112
	AU----703409	B2	19990325		
	ZA---9609486	A	19980512	1996ZA-0009486	19961112
	CN---1202167	A	19981216	1996CN-0198396	19961112
	BR---9611511	A	19990504	1996BR-0011511	19961112
	JP2000500748	T	20000125	1997JP-0518993	19961112
	IL----124487	A	20010111	1996IL-0124487	19961112
	HU---9903459	A2	20010428	1999HU-0003459	19961112
	HU---9903459	A3	20010828		
	TW----422836	B	20010221	TW 1996-85113881	19961113
	AT----319685	T	20060315	1996AT-0308216	19961114
	ES---2258771	T3	20060901	1996ES-0308216	19961114
	NO---9802202	A	19980514	1998NO-0002202	19980514
PRAI	1995US-006864P	P	19951116		
	1996GB-0005434	A	19960315		
	1996WO-US18112	W	19961112		

OS MARPAT 127:66216
GI



I

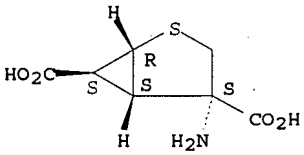
AB Bicyclic amino acids I [X = O, NH, NR, NCOR, S, SO, SO2; R = H or (un)substituted alkyl, alkenyl, alkynyl, aryl, carbocyclyl, heterocyclyl] or their pharmaceutically acceptable salts were prepared for use as modulators of metabotropic glutamate receptor function. Thus, 1SR,4SR,5RS,6SR-4-amino-2-oxabicyclo[3.1.0]hexane-4,6-dicarboxylic acid

was prepared in several steps from 1,2,4-butanetriol and (carbethoxymethylene)triphenylphosphorane. Formulations containing I are described.

IT **191471-53-1P 191471-54-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(excitatory amino acid derivs.)

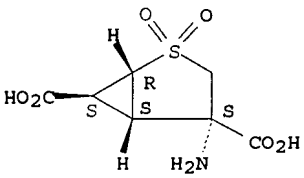
RN 191471-53-1 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 191471-54-2 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, 2,2-dioxide, (1α,4β,5α,6α)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



=> d bib abs hitstr l19 tot

L19 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:665614 HCAPLUS
DN 146:93199
TI The metabotropic glutamate 2/3 receptor agonist LY404039 reduces alcohol-seeking but not alcohol self-administration in alcohol-preferring (P) rats
AU Rodd, Zachary A.; McKinzie, David L.; Bell, Richard L.; McQueen, Victoria K.; Murphy, James M.; Schoepp, Darryle D.; McBride, William J.
CS Department of Psychiatry, Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN, 46202-4887, USA
SO Behavioural Brain Research (2006), 171(2), 207-215
CODEN: BBREDI; ISSN: 0166-4328
PB Elsevier B.V.
DT Journal
LA English
AB Metabotropic glutamate (mGlu) receptors have been shown to mediate a number of behaviors including emotionality and responsivity to stress as demonstrated by efficacy in preclin. and clin. studies. The objective of this study was to assess the effects of the mGlu2/3 receptor agonist LY404039 (LY) on operant ethanol (EtOH) self-administration during alc. seeking (pavlovian spontaneous recovery, PSR), alc. relapse (alc. deprivation effect, ADE), and maintenance responding for alc. Adult alc.-preferring (P) rats were trained in 2-lever operant chambers to self-administer 15% EtOH (volume/volume) and water on a concurrent fixed-ratio 5-fixed-ratio 1 (FR5-FR1) schedule of reinforcement in daily 1 h sessions. After at least 10 wk of daily 1 h sessions, rats underwent seven extinction sessions, followed by 2 wk of no manipulation, and then rats were tested for the expression of an EtOH PSR for four sessions. Rats were then given a week in their home cage before being returned to the operant chambers with access to EtOH and water (alc. relapse). Finally, the effects of LY upon maintenance EtOH and water responding were assessed once stable responding was reestablished. The mGlu2/3 receptor agonist

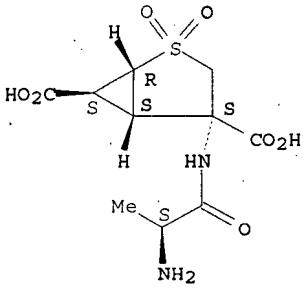
LY404039 reduced responding on the EtOH in the PSR test. LY also reduced the expression of an alc. deprivation effect (ADE) during relapse, but did not reduce EtOH responding under maintenance conditions. The results of this study demonstrate that activating mGlu2/3 receptors inhibits the expression of alc. seeking and relapse behavior without altering alc. self-administration behavior.

IT **611168-14-0**, LY 404039
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(relapseLY404039 inhibited expression of alc. seeking and relapse behavior without altering alc. self-administration behavior in adult alc.-preferring rat)

RN 611168-14-0 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:818322 HCAPLUS
DN 139:302068
TI Therapy for psychoses combining an atypical antipsychotic and an mGlu2/3 receptor agonist
IN Johnson, Bryan Glenn; Schoepp, Darryle Darwin
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2003084610	A1	20031016	2003WO-US07283	20030321
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA---2478227	A1	20031016	2003CA-2478227	20030321
	AU2003218063	A1	20031020	2003AU-0218063	20030321
	EP---1492595	A1	20050105	2003EP-0714045	20030321
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP2005528378	T	20050922	2003JP-0581846	20030321
	US2005192273	A1	20050901	2004US-0509772	20040928
PRAI	2002US-369771P	P	20020403		
	2002US-369797P	P	20020403		
	2003WO-US07283	W	20030321		

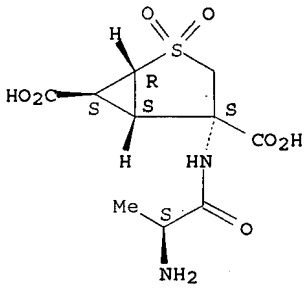
AB The invention provides a pharmaceutical composition and methods for treating psychosis comprising the combination or a first component which is an atypical antipsychotic with a second component which is a mGlu2/3 receptor

agonist. The invention also provides a pharmaceutical composition and method of treating a psychiatric disorder comprising the combination of a first component which is an atypical antipsychotic with a second component which is a compound which allosterically enhances receptor activity for mGlu2 and/or mGlu3.

IT **611168-14-0**, LY 404039 **611168-15-1 611168-20-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotic-mGlu2/3 receptor agonist combination for treatment of psychoses and psychiatric disorders)

RN 611168-14-0 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry.

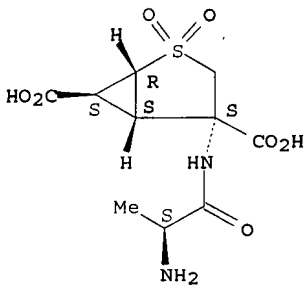


RN 611168-15-1 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)-, mixt. with 8-chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]diazepine (9CI) (CA INDEX NAME)

CM 1

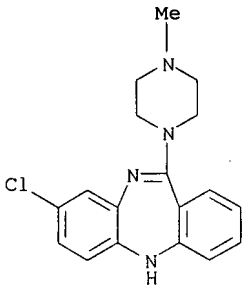
CRN 611168-14-0
CMF C10 H14 N2 O7 S

Absolute stereochemistry.



CM 2

CRN 5786-21-0
CMF C18 H19 Cl N4

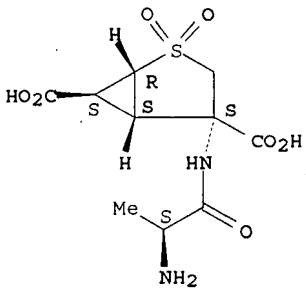


RN 611168-20-8 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-[[(2S)-2-amino-1-oxopropyl]amino]-, 2,2-dioxide, (1R,4S,5S,6S)-, mixt. with 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (9CI) (CA INDEX NAME)

CM 1

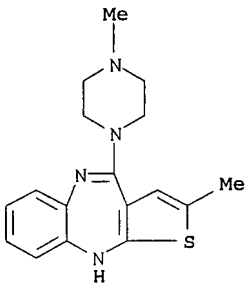
CRN 611168-14-0
CMF C10 H14 N2 O7 S

Absolute stereochemistry.



CM 2

CRN 132539-06-1
CMF C17 H20 N4 S

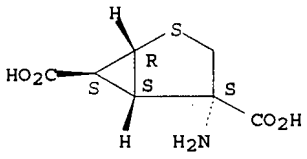


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:769630 HCAPLUS
DN 140:246751
TI Comparison of the effect of glutamate receptor modulators in the 6 Hz and maximal electroshock seizure models
AU Barton, Matthew E.; Peters, Steven C.; Shannon, Harlan E.
CS Lilly Research Laboratories, Neuroscience Research Division, Eli Lilly and

Company, Indianapolis, IN, 46285, USA
SO Epilepsy Research (2003), 56(1), 17-26
CODEN: EPIRE8; ISSN: 0920-1211
PB Elsevier Science B.V.
DT Journal
LA English
AB Glutamatergic ionotropic and metabotropic receptor modulators have been shown to produce anticonvulsant activity in a number of animal seizure models, e.g. maximal electroshock (MES) and DBA/2 sensory-induced seizures. The 6 Hz model of partial seizures is an alternative low frequency, long duration stimulation paradigm resulting in a seizure characterized by jaw and forelimb clonus, immobility, and an elevated tail (Straub-tail). A unique aspect of this model is that it is the only acute elec.-induced seizure model in which levetiracetam has displayed anticonvulsant activity, suggesting that the 6 Hz seizure model may be useful in identifying compds. with unique anticonvulsant profiles. The purpose of the present study was to examine the role of glutamate receptors in the MES and 6 Hz seizure models using a number of NMDA, AMPA/KA, and mGlu receptor modulators. The pharmacol. profile of the 6 Hz seizure model was compared to that of the MES model using eight ionotropic glutamate receptor antagonists and eight mGlu receptor modulators. The ionotropic receptor antagonists MK-801, LY235959, NBQX, LY293558, GYKI 52466, LY300168, and LY377770 produced complete protection from tonic extension in the MES model. Furthermore, the noncompetitive mGlu1 (LY456236) and mGlu5 (MPEP) metabotropic receptor antagonists and the mGlu8 metabotropic receptor agonist (PPG) were also effective in the MES model whereas the competitive mGlu1 (LY367385) receptor antagonist, the mGlu2/3 (LY379268 and LY389795) and Group III (l-AP4) metabotropic receptor agonists were ineffective. In contrast, all of the compds. tested, produced dose-dependent protection in the 6 Hz model with an increase in potency as compared to the MES model. The largest protective indexes (P.I.=TD50/ED50) observed were associated with the iGlu5 antagonist LY382884 and the mGlu2/3 receptor agonists LY379268 and LY389795 (P.I.=>14, 14, and 4.9, resp.) in the 6 Hz model. The results from the present study support the continued search for glutamate receptor modulators as potential antiepileptic agents. Furthermore these results illustrate the importance of using several different animal seizure models in the search for novel AEDs and the potential utility of the 6 Hz seizure model in identifying novel AEDs.
IT **222529-89-7**, LY389795
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of effect of glutamate receptor modulators in 6 Hz and maximal electroshock seizure models)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:851222 HCAPLUS
DN 138:198858
TI Molecular docking of ligands of glutamate receptors
AU Belenikin, M. S.; Makkiarulo, A.; Konstantino, G.; Palyulin, V. A.; Pellichari, P.; Zefirov, N. S.
CS Kafedra Org. Khim., Mosk. Gos. Univ., Moscow, Russia
SO Vestnik Moskovskogo Universiteta, Seriya 2: Khimiya (2002), 43(4), 221-230
CODEN: VMUKA5; ISSN: 0579-9384
PB Izdatel'stvo Moskovskogo Universiteta
DT Journal
LA Russian

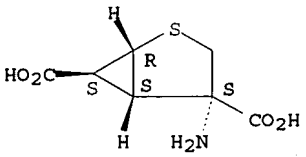
AB Docking of a number of agonists and antagonists into glutamate-binding sites of human metabotropic and ionotropic glutamate receptors was modeled using the computer program AutoDock 3.0. The three-dimensional structures of the ligand-receptor complexes were in good agreement with exptl. data. Effect of water mols. at the ligand-binding site of the receptor on the ligand orientation was studied.

IT **222529-89-7**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(modeling of mol. docking of ligands of human metabotropic and ionotropic glutamate receptors)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L19 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:512140 HCAPLUS

DN 138:198422

TI Group II mGluR receptor agonists are effective in persistent and neuropathic pain models in rats

AU Simmons, Rosa Maria A.; Webster, Amy A.; Kalra, Anshu B.; Iyengar, Smriti

CS Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA

SO Pharmacology, Biochemistry and Behavior (2002), 73(2), 419-427
CODEN: PBBHAU; ISSN: 0091-3057

PB Elsevier Science Inc.

DT Journal

LA English

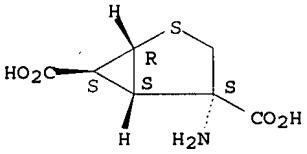
AB The involvement of Group II metabotropic receptors in acute and persistent pain states was evaluated in several in vivo models of pain with selective and potent Group II metabotropic glutamate (mGlu) 2,3 agonists. LY354740, LY379268 and LY389795 attenuated late-phase paw-licking pain behavior in a dose-dependent manner in the formalin model of persistent pain. Effects occurred in the absence of overt neuromuscular deficits as measured by performance in the rotorod test for ataxia. The effects of LY354740 and LY379268 were also stereoselective. The order of potency of the agonists was LY389795>LY379268>LY354740. The attenuation of licking behavior by LY379268 (3 mg/kg) in the formalin model was reversed by a potent and selective mGlu2,3 receptor antagonist, LY341495 (1 mg/kg). In the L5/L6 spinal nerve ligation model of neuropathic pain in rats, LY379268 significantly reversed mech. allodynia behavior in a dose-related manner. In contrast, LY379268 had no significant effects on the tail flick test or paw withdrawal test of acute thermal nociceptive function. These results support the involvement of Group II mGlu2,3 receptors in persistent pain mechanisms and suggest the potential utility of selective Group II mGlu agonists for the treatment of persistent pain.

IT **222529-89-7**, LY389795
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(group II mGluR receptor agonists are effective in persistent and neuropathic pain models in rats)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

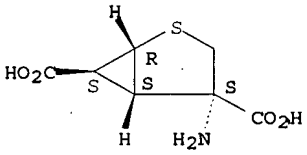
Absolute stereochemistry. Rotation (-).



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:452280 HCAPLUS
DN 137:163325
TI Common and Selective Molecular Determinants Involved in Metabotropic Glutamate Receptor Agonist Activity
AU Bertrand, Hugues-Olivier; Bessis, Anne-Sophie; Pin, Jean-Philippe; Acher, Francine C.
CS Accelrys, Orsay, 91893, Fr.
SO Journal of Medicinal Chemistry (2002), 45(15), 3171-3183
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Several potent and group selective agonists of metabotropic glutamate receptors (mGluRs) have been docked at mGlu1,2,4R binding sites in the closed conformation of the bilobate extracellular domain. Quisqualic acid and (S)-3,5-dihydroxyphenylglycine (3,5-DHPG) were selected for mGlu1R, dicarboxycyclopropylglycine (DCG-IV), LY354740, (S)-4-carboxyphenylglycine (4CPG) for mGlu2R, and (S)-2-amino-4-phosphonobutyric acid (AP4), 1-aminocyclopentane-1,3,4-tricarboxylic acid (ACPT-I), (S)-4-phosphonophenylglycine (PPG) for mGlu4R. The models show a conserved binding pattern for the glycine moiety (α-amino and α-acidic functions) and group specific bindings for the distal acidic function. The best agonists allow optimized interaction with both lobes of the binding domain. Interlobe connections around the ligand are also described and participate in stabilizing the closed form of the amino-terminal domain. Altogether, the docking models support the proposal that the stabilization of a closed state represents a key step in agonist activation of mGluRs.
IT **222529-89-7**, LY 389795
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(common and selective mol. determinants involved in metabotropic glutamate receptor agonist activity)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

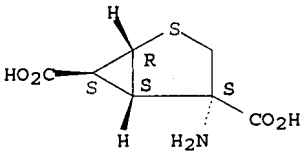


RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:502706 HCAPLUS
DN 135:327224
TI Anti-epileptic activity of group II metabotropic glutamate receptor agonists (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY379268) and (-)-2-thia-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY389795)
AU Moldrich, R. X.; Jeffrey, M.; Talebi, A.; Beart, P. M.; Chapman, A. G.; Meldrum, B. S.

CS Department of Pharmacology, Monash University, Melbourne, 3800, Australia
SO Neuropharmacology (2001), 41(1), 8-18
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier Science Ltd.
DT Journal
LA English
AB The selective group II metabotropic glutamate receptor (mGlu2/3) agonists (-)-2-oxa-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY379268) and (-)-2-thia-4-aminobicyclo[3.1.0]hexane-4,6-dicarboxylate (LY389795) have been evaluated as anti-epileptic drugs in dilute brown agouti (DBA/2) mice, lethargic (lh/lh) mice, genetically epilepsy-prone-9 (GEP) rats and amygdala-kindled rats. Sound-induced clonic seizures in DBA/2 mice were transiently inhibited by both agonists intracerebroventricularly (i.c.v.), LY379268 ED50=0.08 [0.02-0.33] nmol and LY389795 ED50=0.82 [0.27-3.24] nmol or i.p., LY379268 ED50=2.9 [0.9-9.6] mg/kg and LY389795 ED50=3.4 [1.0-11.7] mg/kg. Both mGlu2/3 agonists inhibited seizures induced by the group I mGlu receptor agonist (R,S)-3,5-dihydroxyphenylglycine (DHPG), where LY379268, i.c.v. ED=0.3 [0.02-5.0] pmol and LY389795, i.c.v. ED=0.03 [0.05-0.19] nmol. The spike and wave discharge (SWD) duration of absence seizures in lh/lh mice was significantly reduced by both agonists at 1 and 10 nmol (i.c.v.) up to 90 min following infusion. The elec. induced seizure score and afterdischarge duration of amygdala-kindled rats was partially inhibited by the agonists 30 min after i.p. injection of 10 mg/kg. The agonists did not inhibit sound-induced seizures in GEP rats (0.1-1 mg/kg, 30 min 1 h, i.p.), but were proconvulsant following sound stimulus (≥0.1 mg/kg). These findings identify a potential role for mGlu2/3 agonists in the amelioration of generalized and partial epileptic seizures.
IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-epileptic activity of group II metabotropic glutamate receptor agonists LY379268 and LY389795)
RN 222529-89-7 HCAPLUS
CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:741905 HCAPLUS
DN 133:305610
TI Treatment of neurological disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators
IN O'Neill, Michael John
PA Eli Lilly and Company Limited, UK
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO2000061126	A2	20001019	2000WO-GB01284	20000406
WO2000061126	A3	20010823		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI 1999GB-0008175 A 19990409

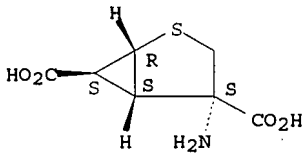
AB The present invention relates to a method of treating a neurol. disorder comprising administering to a patient an effective amount of a nitric oxide synthase inhibitor in combination with an effective amount of an excitatory amino receptor modulator. Combination of 2.5 mg/kg Mk-801, i.p., and 25 mg/kg ARL17477, i.p., had a synergistic degree of neuroprotection (78%) in cerebral ischemia induced in gerbils.

IT **222529-89-7**, LY 389795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

RN 222529-89-7 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L19 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:527203 HCAPLUS

DN 129:156945

TI Treatment for premenstrual dysphoric disorder

IN Levine, Louise R.

PA Eli Lilly and Company, USA

SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO---9832436	A1	19980730	1998WO-US01344	19980123
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA---2275777	A1	19980730	1998CA-2275777	19980123
AU---9862487	A	19980818	1998AU-0062487	19980123
EP---1014971	A1	20000705	1998EP-0904669	19980123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP2001511131	T	20010807	1998JP-0532158	19980123
PRAI 1997US-036176P	P	19970129		
1998WO-US01344	W	19980123		

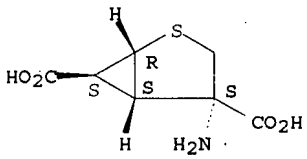
AB Agonists which act at neg.-coupled cAMP-linked metabotropic glutamate receptors are useful for treating premenstrual dysphoric disorder. An example compound which was synthesized is 1SR,4SR,5SR,6SR-4-amino-2-oxabicyclo[3.1.0]hexane-4,6-dicarboxylic acid.

IT **191471-53-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oxa- and thiabicyclohexanedicarboxylates for treatment of premenstrual dysphoric disorder)

RN 191471-53-1 HCAPLUS

CN 2-Thiabicyclo[3.1.0]hexane-4,6-dicarboxylic acid, 4-amino-, (1R,4S,5S,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2 STR L1
L3 4 L2
L4 64 L2 FULL
SAV TEM J559C38/A L4

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E MOHER E/AU
L6 43 E3-6
E MONN J/AU
L7 137 E3-4,E6-8
E TERCERO C/AU
L8 2 E4-5
E PEDREGAL C/AU
L9 58 E3,E5-6
L10 1 US20050222231/PN OR (US2004-516559# OR EP2002-380121 OR EP2002-

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L11 TRA L10 1- RN : 171 TERMS

FILE 'REGISTRY' ENTERED AT 16:50:05 ON 06 AUG 2007
L12 171 SEA L11
L13 36 L12 AND L4

FILE 'HCAPLUS' ENTERED AT 16:50:14 ON 06 AUG 2007
L14 12 L5 AND L6-10
L15 10 L5 NOT L14

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FILE 'HCAPLUS' ENTERED AT 16:53:47 ON 06 AUG 2007
SEL HIT RN L15

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L17 5 L16 NOT P/ELS

FILE 'HCAPLUS' ENTERED AT 16:55:01 ON 06 AUG 2007
L18 17 L17
L19 9 L18 AND L15
SEL AN 4-9
L20 6 E8-19 AND L19
SEL HIT RN

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L21 2 E20-21

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FILE 'REGISTRY' ENTERED AT 16:58:49 ON 06 AUG 2007

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L23          11 L14 NOT L22

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